Pain Research Forum

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Antibiotics May Relieve Some Chronic Low Back Pain, Study Suggests

Low-grade infection of herniated disc may be to blame
by Carol Cruzan Morton on 30 May 2013

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The origin of most chronic low back pain is a mystery to doctors and researchers, but the prevailing theory favors biomechanical instability and prescribes exercise-based care. A pair of new studies advances a remarkable cause and treatment—at least for a select group of people who have had a herniated disc and suffer persistent disability. In these people, one paper suggests, debilitating pain may arise from a troublemaking low-grade infection of the disc by bacteria that usually lurk in hair follicles and are better known for causing pimples. The other study finds that antibiotics may relieve or even prevent the resulting spine degeneration and pain.

"It is an interesting and provocative hypothesis that may turn out to have important applications," said Richard Deyo, a primary care internist who studies back pain at Oregon Health and Science University, Portland, US, and was not involved in the study. The treatment trial has many rigorous research design features, he said, but "before making widespread changes in clinical practice, even a study like this needs to be replicated. There are big stakes in being right about this," said Deyo, referring to the large problem of chronic low back pain, the risky antibiotic side effects in individuals, and the spread of antibiotic resistance.

The two papers on antibiotic treatment and herniated disc infections were published online February 13 in the European Spine Journal by researchers at the Spine Centre of Southern Denmark in Middelfart, and their colleagues.

Bacteria detected, treated

Low back pain is almost as inevitable in a person's lifetime as death and taxes. Fortunately, most people recover within two months with little or no medical intervention. Unfortunately, for

roughly one in 10 people, low back pain becomes a stubborn and sometimes incapacitating problem. Common treatments for low back pain include painkillers and exercise, none of which seem to help much for a subset of long-suffering patients.

The new studies are the latest findings about the connection between back pain and radiology findings called Modic changes (MC) from the Danish Spine Centre group. In the late 1980s, Michael Modic, a neuroradiologist at the Cleveland Clinic, Ohio, US, described three types of degenerative changes at the endplates of vertebrae detected by MRI. Seven years ago, a paper from the Danish group made a splash by linking Modic type 1 changes to back pain (**Kjaer et al., 2006**). The next year, Hanne Albert, the lead author on the new studies, published a study correlating new Modic 1 changes with a previous adjacent disc herniation (**Albert and Manniche, 2007**). Meanwhile, British researchers and others had reported evidence of anaerobic bacteria in herniated discs (**Stirling et al., 2001**). In a pilot study (**Albert et al., 2008**) and the latest papers, Albert tested the idea that infected discs were responsible for potentially painful Modic 1 changes.

In one new paper, an intensive 100-day antibiotic protocol with amoxicillin-clavulanate significantly relieved pain and disability on average compared to placebo, with continued improvement at the one-year follow-up. The double-blinded randomized clinical trial included 162 people with moderate to severe low back pain lasting more than six months who had developed a Modic 1 change in vertebrae adjacent to a previously herniated disc. About half of the treatment group had had disc surgery. At the one-year follow-up, MRI images showed modest shrinking of Modic type 1 changes in the antibiotic group, perhaps suggesting a reversal of painful bone swelling. The findings extend the results of a pilot study testing 32 patients with a similar protocol, published five years ago (**Albert et al., 2008**).

A companion paper reported related results from a separate study looking for evidence of infection in people with back pain. In tissue samples from 61 patients undergoing lumbar disc herniation surgery, nearly half of the normally sterile disc samples tested positive for anaerobic bacteria. Of the people with infected discs, 80 percent developed new Modic 1 changes on the ends of connecting vertebrae within one to two years. Inadvertent sample contamination during surgery is possible but unlikely, contended Albert, a senior researcher at the Spine Centre, based in part on finding only selective anaerobic species, especially *Propionibacterium acnes*, and not other familiar microbes, such as *Staphylococci*.

"The question is not whether or not they're on to something, but how big it is," said Peter Hamlyn, a neurospinal surgeon at the Institute of Sports Exercise and Health at University College London Hospital, UK. Hamlyn was not an author of the papers, but he has treated more than a dozen patients with antibiotics

instead of surgery in the last two years with promising results. He started treating patients with antibiotics after consulting the Danish group about several studies that suggested antibiotics might work for a subset of patients not helped by exercise therapy. "At the moment, there are plenty of holes in the evidence, but certain circumstances warrant treatment in a really tightly controlled and restricted group of patients," he said. "Operations are popular, but they don't always work."

The treatment is not to be taken lightly. The antibiotic regimen poses a risk of severe colitis from a change in normal intestinal flora, which may require hospitalization and intensive therapy with toxic drugs, Deyo said.

Jeffrey Jarvik, a neuroradiologist at the University of Washington, Seattle, US, cautioned that side effects in people on antibiotics may have alerted participants and their caregivers to their treatment or placebo status, unblinding the study. About half of the people on antibiotics suffered diarrhea and other gastrointestinal side effects, or worse. "Because people's expectations play an important role in how they respond to a treatment, especially if the treatment is for pain, unblinding would likely make the active treatment work better and the placebo work worse," he said. Nonetheless, Jarvik said, "In some respects, this would potentially revolutionize the treatment of back pain if the results from this relatively small study were generalizable," because low back pain is so common.

For Hamlyn and others, the new studies evoke the Nobel Prize-winning discoveries that a chronic *Helicobacter pylori* infection of the stomach lining causes 80 to 90 percent of ulcers and the radical change needed for effective, evidence-based clinical care. In contrast, low-grade disc infection probably explains a minority of chronic back pain, said coauthor Claus Manniche, a rheumatologist at the Spine Centre. "It is only a small, specific group who benefit from this," he said. "And it is important they be [treated] by specialists." No one knows exactly how many people have disc herniations, but the antibiotic-worthy combination of herniation, Modic 1 changes, and persistent debilitating pain probably account for no more than 20 percent of people with chronic back pain, he estimates.

Taken together, the papers "strongly suggest one cause of low back pain in combination of MC 1 changes to be of low-grade infectious nature in [the] case of previous disc herniation," wrote Max Aebi, editor-in-chief of the European Spine Journal, in an accompanying editorial in the April 2013 print edition. "Further research is necessary to show what exactly happens in patients with disc herniation who develop MC 1 and low back pain, and who have not been operated on," wrote Aebi, noting the difficulty and importance of determining anaerobic infections in herniated discs of people without surgery.

Looking ahead, Manniche advocates developing new prophylactic guidelines for patients undergoing surgery, including taking a biopsy. "Our studies show that at least 40 percent of the herniated patients lying on the operating table are infected with *P. acnes* bacteria," he wrote in an e-mail. "It is possible that early intervention with antibiotics may thus prevent the infection from becoming chronic pain."

Clinical forecast

Interest in the compelling results is matched or exceeded by worry about the temptation for physicians to expand this antibiotic treatment beyond the narrow indications supported by preliminary evidence. The authors express similar concerns about both reaching people who can benefit and limiting antibiotic treatment to a well-defined group. In partnership with Hamlyn and a UK colleague, several of the authors established a virtual company called **MASTMEDICAL** (Modic Antibiotic Spinal Therapy) to provide training and certification to clinicians and information to patients. For a fee, MASTMEDICAL offers live and online lectures and an exam. When the costs of setting up the website are recouped, MAST will be turned into a nonprofit educational organization, Hamlyn said.

"The idea of MAST is to train people in the totality of the research, warts and all, with the downsides and risks," Hamlyn said. By that standard, MAST may have stumbled earlier this month with the announcement of the research findings. The papers were published online February 13 in the European Spine Journal with little fanfare. They grabbed headlines at a May 7 press conference in London timed with the print publication, sponsored by MAST, and managed without charge by a public relations company. The media invitation to the event from a public relations company began "Announcement of breakthrough medical care for the cause of one of the world's most debilitating diseases," according to a critique of the resulting media coverage headlined "Antibiotics for back pain: hope or hype?" and published in the British Medical Journal (**McCartney, 2013**) (which had run its own positive story a week earlier (**Wise, 2013**). Hamlyn defended the news coverage. "Far from stumbling, we have catapulted an important issue onto the medical research agenda," adding that it was "a great success for patients so often ignored as medically boring."

So what does Modic himself think about the eponymous new antibiotic therapy? Modic forbids residents training with him from using his name to refer to the MRI categories, suggesting "marrow changes" instead. As for the study results, Modic called them "surprising, but they can't be ignored." He is contemplating a study to independently test the prevalence of infection in herniated discs during surgery and the risk of subsequent Modic 1 changes. "We have ascribed these marrow changes after surgery to altered biomechanical forces and accelerated degenerative changes related to the surgery," he

said. "With new evidence, maybe we should entertain the idea that it is more than biomechanical. That said, all good science should be replicable, and all good ideas should be independently tested before acceptance."

Carol Cruzan Morton covers science, health, and the environment, and is based near Boston, Massachusetts, US.

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